

CLAIMS

That which is claimed is:

1. A method for inhibiting growth of a bacterium, the method comprising:
contacting a bacterium with a holin-modified bacteriophage in an amount effective to infect the bacterium;
wherein said contacting results in infection of the bacterium by the holin-modified bacteriophage and inactivation of the bacterium.
2. The method of claim 1, wherein the bacterium is present in or on a non-aqueous matrix.
3. The method of claim 2, wherein the matrix is a solid substrate chosen from cloth, bandage material, a porous substrate, or a non-porous substrate.
4. A method for inhibiting growth of bacteria in an infected subject, the method comprising:
administering to the infected subject a holin-modified bacteriophage, wherein the bacteriophage is administered in an amount effective to infect a bacterium present in a subject and inhibit replication of the bacterium;
wherein said administering is effective to inhibit growth of the bacteria in the subject.
5. The method of claim 4, wherein:
 - a) the holin-modified bacteriophage comprises a mutant holin gene;
 - b) the bacteria in the host are drug resistant bacteria;
 - c) the bacterial infection is present on a body surface; or
 - d) the bacterial infection is at a local site.

6. The method of claim 4, wherein:

- a) said administering is to the local site of infection;
- b) at least two or more different holin-modified bacteriophage are administered to the subject, including wherein at least two of the holin-modified bacteriophage have specificity for different bacterial host cells; or
- c) the subject has a mixed bacterial infection.

7. The method of claim 4, wherein the infecting bacteria is of a genus selected from the group consisting of *Mycobacteria*, *Staphylococci*, *Vibrio*, *Enterobacter*, *Enterococcus*, *Escherichia*, *Haemophilus*, *Neisseria*, *Pseudomonas*, *Shigella*, *Serratia*, *Salmonella*, *Streptococcus*, *Klebsiella* and *Yersinia*.

8. The method of claim 4, wherein the method further comprises administering an antimicrobial agent to the subject.

9. The method of claim 8, wherein the antimicrobial agent is administered prior to administration of the bacteriophage.

10. A pharmaceutical composition comprising a holin-modified bacteriophage and a pharmaceutically acceptable carrier suitable for administration to a human subject.

11. The composition of claim 10, wherein the bacteriophage is in lyophilized form.

12. The composition of claim 10, wherein said composition comprises a mixture of two or more holin-modified bacteriophage.

13. The composition of claim 12, wherein said composition comprises a mixture of two or more different holin-modified bacteriophage that effect inhibition of at least two different bacterial hosts.

14. A method of making a holin-modified phage, the method comprising:
contacting a bacterial production host with a holin-modified bacteriophage, wherein the bacterial production host suppresses early lysis activity of modified holin of the bacteriophage;
wherein infection of the bacterial production host with the holin-modified bacteriophage provides for production of holin-modified bacteriophage progeny.

15. The method of claim 14, wherein the production host suppresses modified holin activity by expression of an anti-holin.

16. The method of claim 14, wherein the production host suppresses modified holin activity by expression of an antisense mRNA which inhibits production of the modified holin.